

## STATUS OF THE CLAIMS

Claims 18-29 are pending in this application and all claims stand rejected. Applicant hereby traverses the rejection.

## REMARKS

The Examiner has maintained all of the rejections previously leveled against the claims at issue, again asserting that the Pinkel *et al* reference both anticipates and makes obvious all of the claims. While Applicant contends that the arguments made in the last filed response should have addressed the Examiner's concerns, Applicant further believes the Examiner is misapplying the Pinkel reference to the invention at hand.

Applicant respectfully asserts that Pinkel describes a method in which the copy number of a DNA sequence of interest is deduced (approximated) from a comparison of the binding of DNA of a subject to at least two nucleic acid sequence target elements (at least one of the nucleic acid sequences being a control sequence and at least one nucleic acid sequence being derived from the sequence of interest) to similarly prepared DNA of a control source. Pinkel states, "[t]hus comparison of the ratios among target elements permits comparison of copy number ratios of different sequences in the probes." (Pinkel Col 3 lines 4 through 6)

In contrast, the methods of the present invention utilize just one nucleic acid sequence (per chromosome) and states, "[a]ny nucleic acid sequence that is unique and representative of a given chromosome may be suitable for the methods of the present invention." (Paragraph 0111, line 6 to 8)

The methods of the present invention then deduce the copy number of the chromosome of interest based on a ratio of the signal from the control DNA and the signal from the subject DNA when each are present in equal amounts and the binding agent is limiting. The specification states, "[t]he method of the present invention is based on the competitive binding, to a limited amount of complementary binding agent, of equal amounts of DNA from a sample and standard of the same organism." (Paragraph 0131, line 1 to 5)

Applicant respectfully asserts that Pinkel never mentions competitive binding and the conclusions in this reference are in no way based on the results of a competitive binding assay. In fact, Pinkel's method would fail if it did not have an excess of immobilized binding agent because if the binding sites were saturated, or nearly saturated, under one set of conditions, the method would not be able to detect an increase in copy number as no more target would bind and no more signal would be detected. Further, Pinkel discloses a concern over the assay principles of linearity and dynamic range and states, "[t]he sensitivity, linearity and dynamic range achievable from the various combinations of fluorochrome and membranes can thus be determined." (Pinkel column 8, lines 48-51). In short, Pinkel does not at all describe a competitive binding assay, let alone an interpretation of the results of such an assay.

Examiner "draws attention to Pinkel from col 2 lines 66 through col 3, line 27 wherein Pinkel describes that comparing binding of reference probes to target elements with the binding of test probe to target elements can detect variations in copy number from normal (due to binding differences)." As stated above, the applicant's method does not use reference probes. The applicants' method also does not attempt to measure binding of reference probes to target elements nor compare the binding of reference probes to the binding of target elements in any way.

As such, Applicant contends that the Pinkel reference discloses a method that is technically distinct from the present invention. In light of the above argument, and further in light of the arguments contained in the prior response and copied in their entirety below, Applicant believes the rejections are improper and respectfully requests that all of the rejections under 35 U.S.C. Sections 102 and 103 be removed and that the claims be placed in a position of allowance.

## **PRIOR ARGUMENTS**

### **1. Rejection of Claims 18 and 26-27 under 35 U.S.C. 102(b)**

The Examiner has rejected claims 18 and 26-27 under 35 U.S.C. 102(b) as unpatentable over Pinkel et al. for the reasons of record.

Applicant respectfully traverses this rejection. Applicant asserts Pinkel et al. describes a method in which equal binding of the sample and the standard to the binding agent produces a detectable signal. In contrast, the methodology described by the rejected claims produces a

detectable signal due to non-equal binding of the sample and the standard to the binding agent. Accordingly, the reference does not teach each and every element of the claimed invention, as required to make a proper rejection under 35 USC 102(b). See *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986).

Moreover, Pinkel et al teaches away from the use of different amounts of test and sample elements and teaches that equal amounts of test and sample elements are required. Also, Pinkel et al teaches away from the use of size, number or fluorescence for multiplexing and teaches the use of only fluorescence intensity for detection. Finally, Pinkel et al does not teach the use of multiple internal controls for fluorescence level testing.

If an independent claim is found to be allowable in an application, all of the claims depending therefrom are allowable as well. Claims 26 and 27 depend from claim 18 and therefore, in view of the foregoing arguments in this response, they are also allowable for the same reasons that independent claim 18 is allowable.

In view of the foregoing, Applicant respectfully requests withdrawal of the Examiner's rejection of claims 18 and 26-27 under 35 U.S.C. 102(b).

## 2. Rejection of Claims 18 and 26-28 under 35 U.S.C. 103(a)

The Examiner has rejected claims 18 and 26-28 under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al. for the reasons of record. Applicant respectfully traverses this rejection.

Initially, Applicant would like to point out that in order for an Examiner to establish a prima facie case of obviousness, the Examiner must show that each and every one of the claim limitations was suggested or taught by the prior art being relied upon. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). When an independent claim is deemed nonobvious under 35 USC 103, then all claims depending therefrom are nonobvious as well. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed Cir. 1988).

Applicant respectfully submits that the Examiner has not overcome this burden. Specifically, all of the claims that were rejected by the Examiner recite non-equal binding of the sample and the

standard to the binding agent. Pinkel et al. does not teach the presence of non-equal binding of the sample and the standard to the binding agent. Accordingly, the Examiner has not overcome the aforementioned burden since each and every one of the claim limitations of the instant invention were not taught or suggested by Pinkel et al.

To establish a *prima facie* case of obviousness under 35 U.S.C. 103(a), the Examiner must show the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209 (Fed. Cir. 1991). In *Amgen*, the Court explained that while the idea may have been “obvious to try,” many pitfalls existed that would have eliminated a reasonable expectation of success.

Applicant submits that the Examiner has not met this burden. In the instant case, one of ordinary skill in the art would have no reasonable expectation of success in modifying Pinkel et al to achieve the teachings of the instant invention. Specifically, Pinkel et al does not teach the presence of non-equal binding of the sample and the standard to the binding agent. Also, Pinkel et al does not teach the use of size, number or fluorescence for multiplexing nor do they teach the use of multiple internal controls for fluorescence level testing. Moreover, Applicant asserts the teachings of Pinkel et al require equal amounts of test and samples whereas in the present invention, this is not necessary. In applying *Amgen* to the instant case, due to the many pitfalls that exist and deficiencies of Pinkel et al compared to the instant invention, one of ordinary skill in the art would not have a reasonable expectation of success in modifying this reference as proposed by the Examiner to achieve the instant invention.

If an independent claim is found to be allowable in an application, all of the claims depending therefrom are allowable as well. Claims 26-28 depend from claim 18 and therefore, in view of the foregoing arguments in this response, they are also allowable for the same reasons that independent claim 18 is allowable.

As such, Applicant respectfully requests that the Examiner withdraw the rejection of claims 18 and 26-28 under 35 U.S.C. 103(a).

### 3. Rejection of Claims 18-21, 23-24 and 26-28 under 35 U.S.C. 103(a)

The Examiner has rejected claims 18-21, 23-24 and 26-28 under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al as applied above, and further in view of Mohammed for the reasons of record. Applicant respectfully traverses this rejection.

Initially, Applicant would like to point out that in order for an Examiner to establish a *prima facie* case of obviousness, the Examiner must show that each and every one of the claim limitations was suggested or taught by the prior art being relied upon. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). “All words in a claim must be considered in judging the patentability of that claim against the prior art.” *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). When an independent claim is deemed nonobvious under 35 USC 103, then all claims depending therefrom are nonobvious as well. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed Cir. 1988).

Applicant respectfully submits that this burden has not been met. The present invention discloses the creation of a detectable signal due to non-equal binding of the sample and the standard to the binding agent. As Applicant has previously pointed out in its response to the rejections above, there are many other aspects of the present invention Pinkel does not teach.

Applicant asserts the aforementioned deficiencies were not taught or suggested by Mohammed et al. Thus, Applicant respectfully submits that the prior art references do not teach or suggest all the limitations of the claims.

Also, to establish a *prima facie* case of obviousness under 35 U.S.C. 103(a), the Examiner must show the proposed modification or combination of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209 (Fed. Cir. 1991). In *Amgen*, the Court explained that while the idea may have been “obvious to try,” many pitfalls existed that would have eliminated a reasonable expectation of success.

Applicant submits that the Examiner has not met this burden. In the instant case, one of ordinary skill in the art would have no reasonable expectation of success in combining Pinkel et al with Mohammed et al to achieve the teachings of the instant invention. Specifically, Pinkel et al does not teach the presence of non-equal binding of the sample and the standard to the binding agent. Also, Pinkel et al does not teach the use of size, number or fluorescence for multiplexing nor does it teach the use of multiple internal controls for fluorescence level testing. Moreover, Applicant asserts that Pinkel et al requires equal amounts of test and samples whereas in the present invention, this is

not necessary. Further, Applicant asserts the aforementioned deficiencies are not taught or suggested by Mohammed et al. In applying *Amgen* to the instant case, due to the many pitfalls that exist, one of ordinary skill in the art would not have a reasonable expectation of success in combining an embryo as taught by Mohammed et al with the disclosure of Pinkel et al to achieve the instant invention.

If an independent claim is found to be allowable in an application, all of the claims depending therefrom are allowable as well. Claims 19-21, 23-24 and 26-28 depend from claim 18 and therefore, in view of the foregoing arguments in this response, they are also allowable for the same reasons that independent claim 18 is allowable.

Thus, Applicant respectfully requests withdrawal of the rejection of claims 18-21, 23-24 and 26-28 under 35 U.S.C. 103(a).

#### 4. Rejection of Claims 18-22, 23-24, 26-28 and 34 under 35 U.S.C. 103(a)

The Examiner has rejected claims 18-22, 23-24, 26-28 and 34 under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al and Mohammed as applied above, and further in view of Ibanez for the reasons of record. Applicant respectfully traverses this rejection.

As previously asserted by Applicant, in order for an Examiner to establish a *prima facie* case of obviousness, the Examiner must show that each and every one of the claim limitations was suggested or taught by the prior art being relied upon. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). When an independent claim is deemed nonobvious under 35 USC 103, then all claims depending therefrom are nonobvious as well. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed Cir. 1988).

Applicant respectfully submits that this burden has not been met. The present invention discloses the creation of a detectable signal due to non-equal binding of the sample and the standard to the binding agent. As Applicant has previously pointed out in its response to the rejections above, there are also many other aspects of the present invention Pinkel does not teach.

Applicant asserts the aforementioned deficiencies were not taught or suggested by Mohammed et al., even in view of Ibanez. Thus, Applicant respectfully submits that the prior art references do not teach or suggest all the limitations of the claims.

Additionally, to establish a *prima facie* case of obviousness under 35 U.S.C. 103(a), the Examiner must show that the proposed modification or combination of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209 (Fed. Cir. 1991). In *Amgen*, the Court explained that while the idea may have been “obvious to try,” many pitfalls existed that would have eliminated a reasonable expectation of success.

Applicant submits that the Examiner has also not met this burden. In the instant case, one of ordinary skill in the art would have no reasonable expectation of success in combining Pinkel et al with Mohammed et al to achieve the teachings of the instant invention. Specifically, Pinkel et al does not teach the presence of non-equal binding of the sample and the standard to the binding agent. Also, Pinkel et al does not teach the use of size, number or fluorescence for multiplexing nor does it teach the use of multiple internal controls for fluorescence level testing. Moreover, Applicant asserts the teachings of Pinkel et al require equal amounts of test and samples whereas in the present invention, this is not necessary. Further, Applicant asserts the aforementioned deficiencies are not taught or suggested by Mohammed et al., even in view of Ibanez. In applying *Amgen* to the instant case, due to the many pitfalls that exist, one of ordinary skill in the art would not have a reasonable expectation of success in combining the teachings of Pinkel et al with Mohammed et al and Ibanez et al to achieve the instant invention.

Furthermore, to establish a *prima facie* case of obviousness under 35 U.S.C. 103(a), the Examiner must show that the prior art relied upon contains some suggestion that would have motivated the skilled artisan to modify a reference or to combine references. *Karsten Mfg. Corp. v. Cleveland Gulf Co.*, 242 F.3d 1376 (Fed. Cir. 2001). Applicant asserts there would be no motivation to combine the teachings Ibanez et al with that of Pinkel et al and Mohammed et al. As previously stated, one of ordinary skill would have no expectation of success in combining Pinkel and Mohammed due to the aforementioned pitfalls and thus no motivation to combine the teachings related to cattle and sheep of Ibanez since they do not overcome the pitfalls.

If an independent claim is found to be allowable in an application, all of the claims depending therefrom are allowable as well. Claims 19-22, 23-24, 26-28 and 34 depend from claim 18 and therefore, in view of the foregoing arguments in this response, they are also allowable for the same reasons that independent claim 18 is allowable.

As such, Applicant respectfully requests withdrawal of the rejection of Claims 18-22, 23-24, 26-28 and 34 under 35 U.S.C. 103(a).

5. Rejection of Claims 18-21 and 23-28 under 35 U.S.C. 103(a)

The Examiner has rejected claims 18-21 and 23-28 under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al and Mohammed et al as applied above, and in light of Gvakharia. Applicant respectfully traverses this rejection.

Initially, Applicant would like to point out that in order for an Examiner to establish a *prima facie* case of obviousness, the Examiner must show that each and every one of the claim limitations was suggested or taught by the prior art being relied upon. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). “All words in a claim must be considered in judging the patentability of that claim against the prior art.” *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). When an independent claim is deemed nonobvious under 35 USC 103, then all claims depending therefrom are nonobvious as well. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed Cir. 1988).

Applicant respectfully submits that this burden has not been met. The present invention discloses the creation of a detectable signal due to non-equal binding of the sample and the standard to the binding agent. As Applicant has previously pointed out in its response to the rejections above, there are also many other aspects of the present invention Pinkel does not teach.

Applicant respectfully asserts the aforementioned deficiencies are not taught or suggested by Mohammed et al or Gvakharia et al. Thus, Applicant respectfully submits that the prior art references do not teach or suggest all the limitations of the claims.

Furthermore, to establish a *prima facie* case of obviousness under 35 U.S.C. 103(a), the Examiner must show that the proposed modification or combination of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the



time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209 (Fed. Cir. 1991). In *Amgen*, the Court explained that while the idea may have been “obvious to try,” many pitfalls existed that would have eliminated a reasonable expectation of success.

Applicant asserts the Examiner has not met this burden. In the instant case, one of ordinary skill in the art would have no reasonable expectation of success in combining Pinkel et al with Mohammed et al to achieve the teachings of the instant invention. Specifically, Pinkel et al does not teach the presence of non-equal binding of the sample and the standard to the binding agent. Moreover, Pinkel et al does not teach the use of size, number or fluorescence for multiplexing nor does it teach the use of multiple internal controls for fluorescence level testing. Also, Applicant asserts the teachings of Pinkel et al require equal amounts of test and samples whereas in the present invention, this is not necessary. Further, Applicant respectfully asserts the aforementioned deficiencies are not taught or suggested by Mohammed et al or by Gvakharia et al. The Examiner has cited Gvakharia to argue that it discloses an embryo sample originating from a blastomere. In applying *Amgen* to the instant case, due to the many pitfalls that exist, one of ordinary skill in the art would not have a reasonable expectation of success in combining Mohammed et al with Pinkel et al and further combining that with a blastomere as taught by Gvakharia et al to achieve the instant invention. Applicant submits that none of the aforementioned pitfalls can reasonably be expected to be overcome by the addition of a blastomere.

Furthermore, to establish a *prima facie* case of obviousness under 35 U.S.C. 103(a), the Examiner must show that the prior art relied upon contains some suggestion that would have motivated the skilled artisan to modify a reference or to combine references. *Karsten Mfg. Corp. v. Cleveland Gulf Co.*, 242 F.3d 1376 (Fed. Cir. 2001). In light of the foregoing paragraph and analysis, there would be no motivation to combine the teachings Gvakharia et al with that of Pinkel et al and Mohammed et al. As previously stated, one of ordinary skill would have no expectation of success in combining Pinkel and Mohammed due to the many pitfalls and thus no motivation to combine the teaching related to blastomeres of Gvakharia since they do not overcome any of the aforementioned pitfalls.

If an independent claim is found to be allowable in an application, all of the claims depending therefrom are allowable as well. Claims 19-21 and 23-28 depend from claim 18 and therefore, in view of the foregoing arguments in this response, they are also allowable for the same reasons that independent claim 18 is allowable.

As such, Applicant respectfully requests withdrawal of the rejection of Claims 18-21 and 23-28 under 35 U.S.C. 103(a).

6. Rejection of Claims 18 and 26-29 under 35 U.S.C. 103(a)

The Examiner has rejected claims 18 and 26-29 under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al as applied above and in further view of Bitner. Applicant respectfully traverses this rejection.

Initially, Applicant would like to point out that in order for an Examiner to establish a *prima facie* case of obviousness, the Examiner must show that each and every one of the claim limitations was suggested or taught by the prior art being relied upon. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). “All words in a claim must be considered in judging the patentability of that claim against the prior art.” *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). When an independent claim is deemed nonobvious under 35 USC 103, then all claims depending therefrom are nonobvious as well. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed Cir. 1988).

Applicant respectfully submits that this burden has not been met. The present invention discloses the creation of a detectable signal due to non-equal binding of the sample and the standard to the binding agent. As Applicant has previously pointed out in its response to the rejections above, there are also many other aspects of the present invention Pinkel does not teach.

Also, to establish a *prima facie* case of obviousness under 35 U.S.C. 103(a), the Examiner must show that the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209 (Fed. Cir. 1991). In *Amgen*, the Court explained that while the idea may have been “obvious to try,” many pitfalls existed that would have eliminated a reasonable expectation of success.

Applicant submits that the Examiner has not met this burden. In the instant case, one of ordinary skill in the art would have no reasonable expectation of success in modifying Pinkel et al to achieve the teachings of the instant invention. Specifically, Pinkel et al does not teach the presence of non-equal binding of the sample and the standard to the binding agent. Also, Pinkel et al does not teach the use of size, number or fluorescence for multiplexing nor does it teach the use of multiple

internal controls for fluorescence level testing. Moreover, Applicant respectfully asserts the teachings of Pinkel et al require equal amounts of test and samples whereas in the present invention, this is not necessary. In applying *Amgen* to the instant case, due to the many pitfalls that exist and deficiencies of Pinkel et al compared to the instant invention, one of ordinary skill in the art would not have a reasonable expectation of success in modifying this reference as proposed by the Examiner to achieve the instant invention.

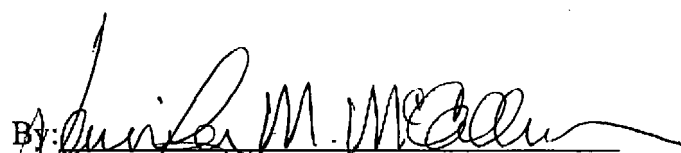
Further, Applicant respectfully asserts combining Bitner et al with Pinkel et al would not make the resulting invention capable of overcoming any of the aforementioned pitfalls. Even if the silanized silica microparticles of Bitner were combined with Pinkel, one of ordinary skill would not have any expectation of success in achieving the instant invention due to the fact, among others, that neither reference teaches or suggests the presence of non-equal binding or the use of unequal amounts of test and samples.

If an independent claim is found to be allowable in an application, all of the claims depending therefrom are allowable as well. Claims 26-29 depend from claim 18 and therefore, in view of the foregoing arguments in this response, they are also allowable for the same reasons that independent claim 18 is allowable.

As such, Applicant respectfully requests withdrawal of the rejection of Claims 18 and 26-29 under 35 U.S.C. 103(a).

In view of the foregoing, Applicant respectfully contends that all claims are in a condition for allowance. If the Examiner notes any further matters which would be expedited by a telephonic interview, he or she is requested to call Dr. Jennifer M. McCallum at the telephone number listed below.

Respectfully submitted,

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